HCCA Conference

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Navigating Animal Research Compliance and Managing Risk

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OBJECTIVES

- Overview of animal research regulations and organizations.
- Overview of the IACUC.
- Overview of PAM.
- Describe trends and challenges of Post-Approval Monitoring Programs (PAM).
- Identify risks affecting animal research and discuss strategies to implement corrective and preventative actions.
- Discuss strategies for minimizing and mitigating risks.

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"Unlike human participants, animals will never be able to consent to experimental procedures. Accordingly, ethical evaluation ought to be very stringent to protect animals from unnecessary harm."

-L. Houde, C. Dumas and T. Leurox.

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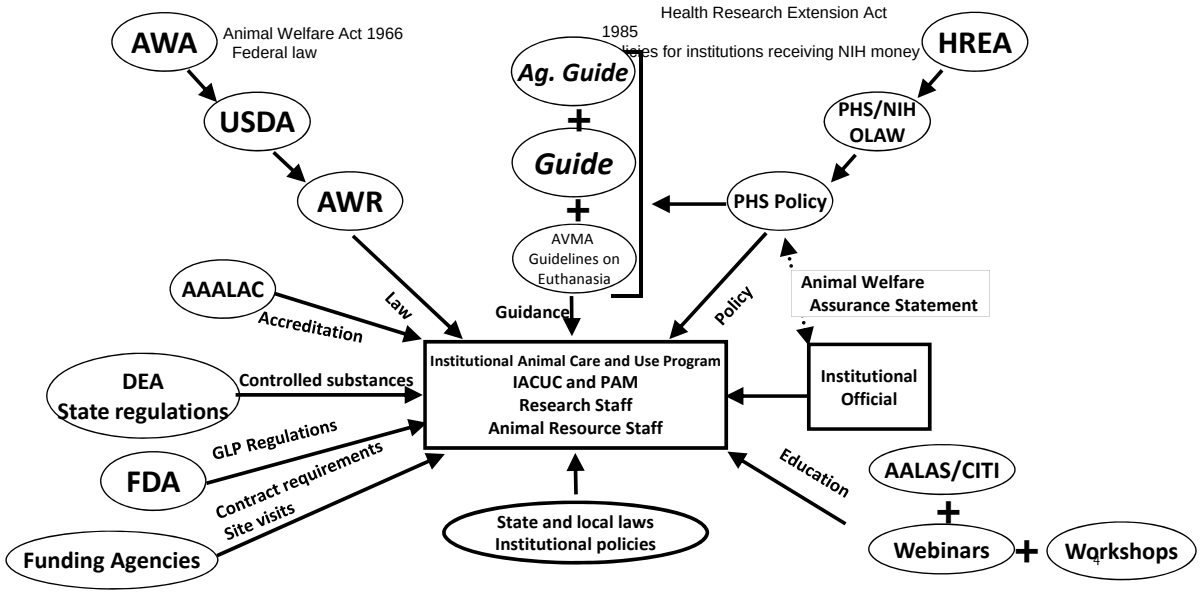
ANIMAL RESEARCH REGULATIONS



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- **Private, nonprofit that promotes the humane treatment of animals in science.**
- **Voluntary accrediting organization.**
- **Many funding agencies require AAALAC accreditation.**
- **Site visits every three years for accreditation.**
- **Institutions are required to submit a Program Description prior to their site visit.**
- **The *Guide,* Ag Guide and AWARs as primary standards for assessing accreditation status.**

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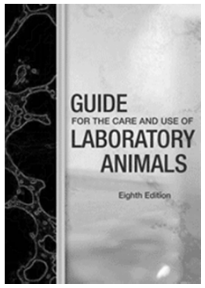
NATIONAL INSTITUTE OF HEALTH (NIH) OFFICE OF LABORATORY ANIMAL WELFARE (OLAW)

- **NIH/OLAW oversee the implementation of the Health Research Extension Act of 1985 (Must comply with the PHS policy).**
- **Applies to all live, vertebrate animals (fish, amphibians, reptiles, birds and mammals).**
- **Required for PHS-funded research.**
- **The *Guide* is to be used "as a basis for developing and implementing an institutional program for activities involving animals".**
- **Animal Welfare Assurance**



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THE UNITED STATES DEPARTMENT OF AGRICULTURE (USDA)

- **Responsibility for compliance with AWA and AWAR is granted to APHIS/AC.**
- **AWA is enforced through licensing, registration, cooperation from licensees and other organizations and unannounced inspections.**
- **Regulate warm-blooded animals alive or dead (exclude common lab mice and rats, birds bred specifically for research, and farm animals that are used for food or fiber or food or fiber research).**
- ***Animal Care Policy Manual* is a series of policies that provide guidance for AWA and AWARs. "Interpretative Rules".**

USDA Animal Care

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THE INSTITUTIONAL OFFICIAL (IO)

- **Appointed by the CEO.**
- **"The individual who, as a representative of senior administration, bears ultimate responsibility for the Program and is responsible for resource planning and ensuring alignment of Program goals with the institution's mission." (Guide, p. 13)"**
- **Has the authority to assure that AWA/AWARs and PHS Policy requirement and standards be met.**
- **The IACUC reports the status of the animal care and use program to the IO.**
- **The IO has the option to not allow an IACUC approved protocol to proceed; however the IO can not approve a protocol the IACUC disapproved.**

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THE IACUC

- Appointed by the CEO or delegated official.
- Two functions:
  - To ensure institution remains in compliance with laws, regulations and policies.
  - To ensure the welfare of animals used in research, testing or teaching.
- Responsibilities include:
  - Approve research protocol.
  - Approve proposed changes to protocols.
  - Semi-annual inspection of animal facilities, review of animal care and use program and reports to the IO.
  - Investigate complaints about animal care and use.
  - Suspend animal use activities.
  - Advise the IO with regard to animal care and use.

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THE ATTENDING VETERINARIAN "VOICE OF THE ANIMALS"

- Has training in the care and management of the animal species being used at an institution.
- Has authority to represent the institution's animal care and use program.
- Person immediately responsible for the animal care and use program.
- Offers the IACUC the expertise of medical and surgical matters including anesthesia, analgesia and euthanasia procedures.

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PRINCIPAL INVESTIGATOR

- **Principal Investigator is the critical link among:**
  - **IACUC/Institution**
  - **Research team**
  - **Ancillary staff**
  - **Animal care staff**
  - **Compliance staff**
  - **Regulatory agencies**
  - **Sponsor**
- **Responsible for all aspects of the approved animal protocol.**
  - **Oversight of the research.**
  - **Ensure all staff is adequately training.**
  - **Compliance with all protocols, regulations and policies.**
  - **Addressing any concerns associated with the research.**

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THE IACUC ANIMAL USE PROTOCOL FORM

- **Institutional form that describes animal research experiments that an investigator wishes to perform.**
- **The IACUC reviews and either approves, disapprove or requires modifications to the protocol.**
- **The Animal Use Protocols must be compliant with**
  - **The PHS Policy**
  - **The Guide**
  - **The AWA/AWRS**
  - **AAALAC Program Description**
  - **AVMA Panel on Euthanasia**
  - **State and Institutional regulations**

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PAIN CATEGORIES

B No Pain or Distress	C Slight or momentary pain or distress or no pain or distress	D Pain or distress appropriately relieved by analgesia, tranquilization or anesthesia.	E Unrelieved pain or distress
Animals being maintained without any research manipulation.	Holding, weighing or transporting animals (relatively short distances under non-stressful conditions)	Survival/terminal surgical procedures	Burns or trauma
Observation of animal behavior	Injections (nonirritating)	Any post procedural outcome resulting in evident pain, discomfort or distress	Application of noxious stimuli (i.e. electrical shock) that cannot be avoided or escaped
Physical restraint	Blood collection or catheterization of superficial vessels	Genetically engineered phenotype that causes pain or distress that will be alleviated.	Toxicological or microbiological testing, cancer research or infectious disease research that requires continuation until clinical symptoms are evident or death occurs.
Routine husbandry procedures	Collection of body fluids or tissues post mortem	Exposure of blood vessels for catheter implantation	Exposure to abnormal or extreme environmental conditions

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Office of Laboratory Animal Welfare
OLAW

WHY POST-APPROVAL MONITORING ?

- PHS Policy
  - Continuing IACUC oversight of animal activities is required.
  - Monitoring animal care and use is required by the PHS Policy.
  - Semi-Annual Program Review and Facility Inspection.
- USDA
  - The IACUC is responsible for the appropriate monitoring of animal use activity at the research facility [2.31(d)(5)].
  - The IACUC shall conduct continuing reviews of activities . . . at appropriate intervals as determined by the IACUC, but not less than annually. 2.31(d)(5).

USDA Animal Care

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WHAT PAM IS..

- Ensure animal well being.
- Protect the organization.
- Ensure regulatory compliance.
- Provide educational opportunities.
- Resource for the research community.
- Facilitate science and help achieve compliance.

- To ensure that research activities involving animal subjects are conducted in a manner utilizing ethical principles that protects the safety, rights, and welfare of the animals.

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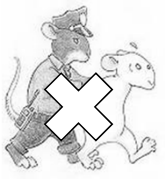

WHAT PAM IS NOT..

- Not the animal police.
- Not a replacement for the Institutional Official, IACUC or Veterinary Staff.
- Not an opportunity for "attack".
- Not required by USDA or PHS.
- Not an AAALACi "MUST".
- Not something new.

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WHO?

- Post Approval Monitor/Compliance Liaison
- Principal Investigator and Research Staff
- Animal Care Technicians/Veterinary Staff
- IACUC Staff/Committee
- Institutional Official
- Institutional/Organizational Leadership
- Committees:
  - Institutional Biosafety
  - Radiation Safety
  - Chemical Safety
  - Occupational Health and Safety
  - Infection Control
- Sponsors/Funding Agencies
- Facility managers
- Teamwork is crucial to the success of a PAM Program.
- 4CS: Collegial, Collaborative, Committed Communicative

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WHERE?

- Wherever Animals Go, So Should PAM!!
- Walk the same path.

- Animal Facility
- Investigator's Labs
- Collaborator's Facilities

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WHEN?

- **Routine**
  - The purpose of this visit is simply to collect evidence of good performance.
  - The reviews are designed to provide researchers and their study teams with immediate feedback on matters of protocol adherence and regulatory compliance.
- **For-Cause**
  - At the request of organizational leadership, the IACUC or the AV, PAM may conduct a focused review of issues and concerns raised by any of these individuals.

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REPORTING AND DATABASE MANAGEMENT

- **Computer database, Spreadsheets or PAM software programs are critical to keep the PAM Program organized, track results and identify trends.**

- **Trending allows for the opportunity to identify strengths and weaknesses in an animal program. "RISK ASSESSMENT"**
- **Tailor training programs towards areas with high incidences of non-compliance.**

- **Best to identify the systems that are currently being used at your institution especially those used with the IACUC and animal care/veterinary staff.**

Development of standardized templates, correspondence and checklists are important.

REDCap™ Research Electronic Data Capture

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HOW?

- Four general models are:
  - Attending-Veterinarian (AV) based
  - IACUC staff/members based
  - Hybrid model
  - Compliance office-based

- Decision to choose which model to follow will depend on your organizational structure, institutional goals, current compliance status and culture, size of the animal program, number of animal use locations, number of researchers, types of species and budgets.

- Observational Review
- Protocol/Record/SOP/Policy/Guideline Review

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PROCESS

- Protocols selected based on risk: Pain/Distress Category, Species, Unique/Innovative Model, Survival Surgery, Food/Fluid Restriction, Prolonged Restraint, Past Compliance History.
- Protocol Review.
- Training Review.
- Introductory meeting with PI and study team. Schedule in advanced, avoid drop-ins.
- Procedural/Surgical Observation.
- Document Review (surgical and post-surgical records).
- Exit meeting with PI, study team, animal care and/or veterinary staff. Briefly review observations and recommendations.
- Follow up with a report to the PI and to the IACUC.

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"RISKY BUSINESS"

- IACUC Protocols are selected for PAM review based on risk:
  - Pain/Distress Category: All category E protocols are reviewed annually.
  - Species: All USDA species protocols are reviewed annually.
- Unanticipated adverse incidents will trigger a PAM review.
- Incorrect or incomplete records will trigger a PAM review.

Unique/Innovative Model
Multiple Survival Surgery
Food/Fluid Restriction
Prolonged Restraint
Past Compliance History

→ Frequency of the review will occur based on direction from the IACUC and veterinary staff.

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"RISKY BUSINESS"

- Keep our institution off the front page of the newspaper.
- Keep the IO out of Jail.
- Avoid fines.
- Avoid tarnished reputation.

Sometimes you just gotta say "what the heck."

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RISKS ASSOCIATED WITH ANIMAL RESEARCH

- **Occupational exposure to biological, chemical hazards, allergens**
  - **Research Safety Program, Occupational Health Program, Personal Protective Equipment**
- **Zoonotic diseases**
- **B-virus exposure (NHP), Q-fever exposure (Sheep)**
  - **Occupational Health and Safety Program, Personal Protective Equipment**
- **Loss of animals due to mechanical failures (HVAC)**
  - **Disaster Response Plan**
- **Loss of animals due to disease outbreak, extreme weather, fire**
  - **Sentinel program, Health surveillance program**
- **Break in, Animal rights activity**
  - **Disaster Response Plan**

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ANIMAL CARE AND USE PROGRAM RISKS

- **Institutional history.**
- **Inter-institutional collaborations MOUS ARE A MUST!!!**
- **Innovative research with USDA species**
- **Oversight of innovative research with USDA species**
- **NHP program**
- **Protocol noncompliance**
- **Humane endpoints**
- **Post-procedure monitoring**
- **Category E studies**
- **Weaknesses within IACUC protocol system**
- **Lack of standardization of procedures, analgesia/anesthesia plans**

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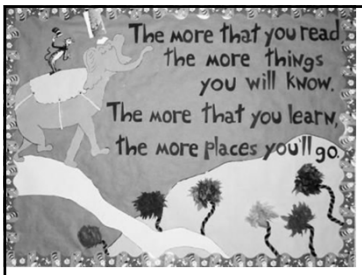

ANIMAL CARE AND USE PROGRAM RISKS

- **Continued communication with your colleagues.**
- **Stay in the loop with list-serves USDA, IACUC-Admin, COMP-MED, etc.**
- **Attend conferences, webinars, seminars.**
- **Top areas of deficiencies are noted by OLAW, AAALAC, USDA.**

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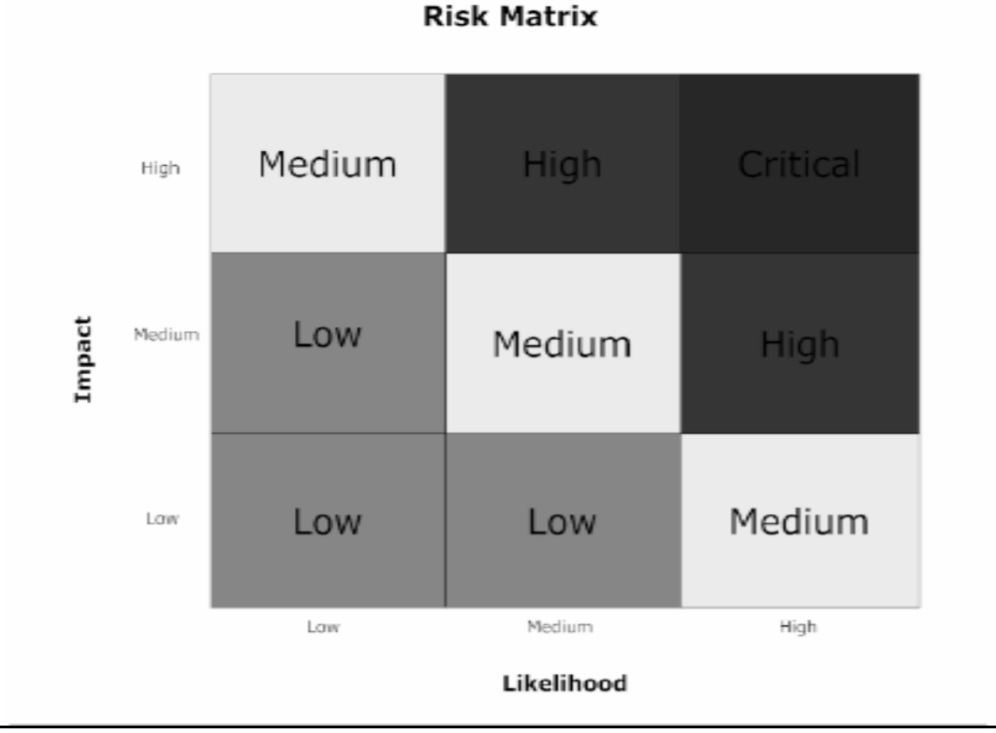

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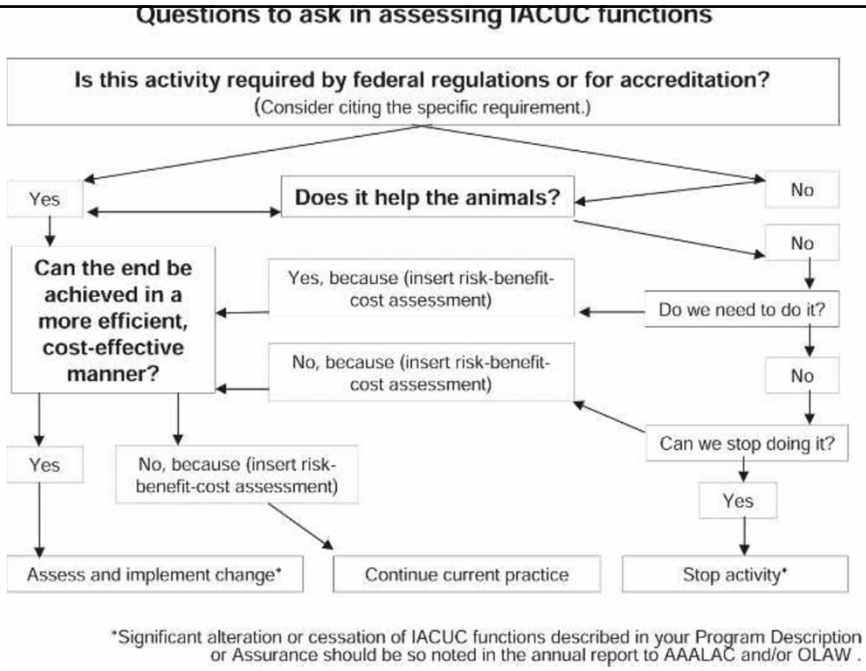

Haywood and Greene. 2008. Avoiding and Overzealous Approach: A Perspective on Regulatory Burden. ILAR J 49:426-434

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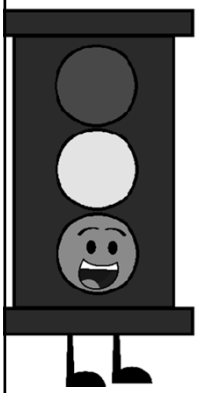
RISK AND YOUR INSTITUTION

- **What level of risk will be accepted?**
- **How will the risk be controlled**
  - **Avoidance, Transference/Sharing, Prevention, Reduction, Acceptance.**
  - **Actions can be risk specific.**



- **Prevention and Reduction are how the majority of institutions choose to handle risk.**
  - **PAM, Training, SOPs and Policies, Veterinary Oversight, Pilot studies,**

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FIFI^2: "FIND IT, FIX IT BEFORE THE FEDS FIND IT, FINE IT"

- **Causes of Noncompliance:**
  - **Inadequate training (techniques, recordkeeping)**
  - **Inadequate record keeping**
  - **Failure to adhere to IACUC approved protocol, institutional policies**
  - **Inadequate or lack of guidance (unclear or lack of institutional policies, SOPs and guidelines)**
  - **Unrealistic expectations or policies**
  - **Inadequate oversight by PI or senior research staff.**
  - **Cultural differences and animal use perspective**
  - **Institutional culture (punitive versus collaborative, "gotcha mentality")**
  - **Division/department/research lab culture**
  - **Lack of IACUC or veterinary support**

- **Non-compliant items discovered during PAM visits are communicated to the PI/research staff, AV, IACUC chair, IACUC, IO and compliance department.**

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REPORTING NON-COMPLIANCE – THE AWA

What is reportable?

- **Any significant deficiency which is not corrected within a reasonable time.**
- **Suspension of any activity involving animals.**

Non-compliance must be reported to

- **APHIS**
- **Any federal agency funding the reported activity.**
- **AAALAC.**

Reporting Non-compliance – The PHS Policy

What is reportable?

Any serious or continuing non-compliance with the Policy.

- **Any serious deviation from the Guide.**
- **Any suspension of activity by the IACUC.**

Reports must include

- **A full explanation of circumstances.**
- **Actions taken.**

Non-compliance must be reported to

- **OLAW**
- **Funding Agency**
- **AAALAC**

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NON COMPLIANCE AND THE AFTERMATH "REMIX IT"

- Always have a process for handling non-compliance in place and review it periodically. (Policy!!)
- Invite research team to an IACUC meeting.
- Voluntary cessation of experiments by research team.
- Protocol amendments.
- Retraining opportunities
  - AALAS/CITI on-line training modules
  - In-person training with veterinary staff, IACUC or compliance staff
  - Attendance at external training opportunity (IACUC 101), Charles River or Jackson hands on course, PRIMR, AALAS.
  - Training consultants
  - PHS and APHIS website
  - APHIS AWIC course
  - AALAS Publications and IACUC literature

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METHODS/STRATEGIES FOR ENSURING COMPLIANCE

- **Investigator oversight**
- **Education and training**
- **Monitoring and auditing**
  - **Internal audit**
- ***Corrective* and *preventive* action plans**
- **Regulatory and Protocol Compliance**
- **Understanding role and responsibilities RACI**
- **Documentation of training**
- **Accurate and complete recordkeeping**
- **Standard Operating Procedures(SOPs)**
- **Rapid response by the team of any findings of deficiencies**
- **Monitoring tools and resources**
  - **Self Audit Checklist**
  - **Investigator's Guide**

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TIPS FOR A SUCCESSFUL PAM PROGRAM

- **Stay Organized.**
- **Keep It Simple.**
- **Be a Liaison.**
- **Communicate, Communicate, Communicate!**
- **Network.**
- **Remember that PAM is a Process, a strong program takes trial and error.**
- **Review your program regularly, don't be afraid to make changes.**
- **Developing collegial collaborations among all PAM participants is crucial for the success of the program.**

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